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EXAMINER	
BASI, NIRMAL SINGH	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,338	KANNO ET AL.	
	Examiner	Art Unit	
	Nirmal S. Basi	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7 and 9-16* is/are pending in the application.

4a) Of the above claim(s) *1-4 and 9-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7, 15-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment filed 7/9/04 has been entered. Applicant has cancelled claims 5, 6 and 8, amended claim 7, and added new claims 15 and 16. Claims 1-4 and 9-14 were withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention (see previous Office Action). Newly added claims 15 and 16 will be examined, together with amended claim 7, as they pertain to the elected invention of Group II.

2. ***Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st paragraph***

The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 7 remains rejected and newly added claims 15 and 16 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

A "specific utility" is a utility that is specific to the subject matter claimed, as opposed to a "general utility" that would be applicable to the broad class of the

invention. A "substantial utility" is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. A "well established utility" is a utility that is well known, immediately apparent, or implied by the specifications disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. A "well established utility" must also be specific and substantial as well as credible.

Based on the record, there is not a "well established utility" for the claimed invention. Applicant has asserted utilities for the specifically claimed DNA and protein of claims 7 , 15 and 16.

Applicant's arguments are summarized below. Applicant argues:

The asserted utility of the claimed gene and protein of the present invention is that they are useful for breeding of a microorganism for the purpose of modifying transport of amino acids across a cell membrane. The claimed gene and protein are members of a family of genes/proteins which are known in the art to be useful as ATP binding cassette transporters (ABC transporters). The ATP transporters have an established physiological function of uptake and excretion of substances into and out of the cell. This is an important and defined function in the cell machinery, allowing a cell to excrete toxic and unneeded substances, while importing useful substances for its metabolism. Transporters have a defined and credible usefulness which is practical in that these proteins can be expressed in a cell and effect the transport of substances, and in the instant invention, amino acids, inside and outside of the cell. Any person of

ordinary skill in the art would recognize this utility as useful in its currently available form and not merely an object of further use testing

Applicants arguments have been fully considered but not found persuasive for the reason given below:

Based on the record, there is not a "well established utility" for claimed ABC transporter because the amino acids transported by claimed invention have not been disclosed. The ABC transporters comprise a family of functionally and pharmacologically diverse compound transporters with diverse effects (see Higgins, IDS ref AAA).

Higgins, (page 68 and Table 1), discloses that the designation ABC transporters recognizes a highly conserved ATP-binding cassette, which is the most characteristic feature of this super family. Some ABC transporters require an associated periplasmic receptor for uptake, others do not. Some ABC transporters have a role in multidrug resistance, others do not. Over 50 ABC transporters are known. Typically, ABC transporters utilize the energy of ATP hydrolysis to pump substrates across the membrane against a concentration gradient , but again there are exceptions. Each ABC transporter is relatively specific for a given substrate. ABC transporters are specific for amino acids, sugars, inorganic ions, polysaccharides, peptides, and even proteins have been characterized (Table 1). Some ABC transporters are uptake (import) systems that accumulate substrate within the cell, while others export substrate from the cell, none has been identified that can pump in both directions.

Further, page 78, Higgins discloses, comparison of the amino acid sequences of the transmembrane domains of one transporter with those of another reveals little or no significant similarity (except for a few specific cases). The only significant sequence conservation between the transmembrane domains of several different ABC transporters is a short motif identified on many bacterial transporters. Sequence similarity has been detected between the yeast STE6 peptide transporter and Hlyb hemolysin exporter, and human P-glycoprotein (all transport different compounds)

On page, 86 Higgins discloses, ABC transporters have been identified for almost every class of substrate imaginable, including sugars, peptides, inorganic ions, amino acids, oligopeptides, polysaccharides, and proteins (Table 1). Not only are these substrates chemically very different, but they also vary enormously in size. The mechanism by which such diversity is achieved, while each transporter retains a high degree of selectivity for its own particular substrate, 'presents an intriguing problem. ' .

On page 88, Higgins discloses, even close similarities between ABC transporters can be misleading: the Mal and Ugp transport systems of E. coli are closely related yet handle different substrates and the two human mdr genes are very similar to each other, yet only one is able to mediate drug transport.

The specification does not disclose the compounds transported by claimed transporter. The prior art discloses that the substrate transported cannot be determined based on sequence homology. It is not even clear if claimed invention is an import or an export system. Does the claimed ABC transporter import or export amino acids, sugars, inorganic ions, polysaccharides, peptides or some other compound. Will the

export or import of a compound be useful for breeding of a microorganism for the purpose of modifying transport of amino acids across a cell membrane. There are no examples provided in the specification or prior art where the claimed ABC transporter of SEQ ID NO:9 has been used for the purpose of breeding of a microorganism for the purpose of modifying transport of amino acids across a cell membrane.

Therefore the utilities asserted by Applicant are not specific or substantial. Neither the specification nor the art of record disclose the protein of SEQ ID NO:9 encoded by the DNA of SEQ ID NO:7 or fragments thereof useful for the purpose of breeding of a microorganism for the purpose of modifying transport of amino acids across a cell membrane. There is no disclosure of the beneficial affects of claimed transporter in bacteria which can be utilized for breeding. Thus the corresponding asserted utilities for the ABC transporter, with no disclosed ligands or compounds which it transports, are essentially methods of treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. It would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the ABC protein/DNA and fragments thereof, further experimentation is necessary to attribute a utility to the claimed invention. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a

hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

The specification discloses the claimed ABC protein/DNA is related to other proteins of the ABC transporter family. Applicant has used the homology to form the basis for utility for the claimed ABC protein/DNA. There is no disclosure in the art that proteins which have the homology disclosed in the specification are "sufficiently similar" and have the same function or transport the same compounds. It is unlikely, based on the art and Applicants specification that the ABC transporters comprise a family of functionally and pharmacologically diverse compound transporters with diverse effects. Therefore, the first question is, to which family of proteins does ABC belong, and secondly which particular member of the family has the same identical activities, functions and pharmacological of the ABC transporter of SEQ ID NO:9. The specification provides no clear answers. There is no disclosure of when a protein is considered "sufficiently similar" to be considered having all the properties of a family or of a specific species. There is no disclose in the specification of the percent identity to related family members to assign functionality. Applicant has made sequence related predictions based on a limited homology between proteins, and based utility arguments on the family of proteins that have shown the closest identity. Based on the diversity of activity, functionality and ligand specificity of the ABC transporter family further experimentation is required to attach a specific function to the claimed ABC transporter. The specification does not disclose the specific function of the claimed ABC transporter, the transporter mechanism involved in movement of molecules across cell membranes,

and the cytotoxic agents or ions that are moved. There is no disclosure by which claimed ABC transporter function, the utility in testing for its ability to confer drug resistance on cells expressing ABC (either normally or artificially), is based, or what specific drugs or ligands effect what specific transport, in cells expressing ABC, which in turn leads to utility in breeding. There is no disclosure of the scientific reasoning, that sequence similarity, in instant case, between claimed ABC transporter and other proteins that can be used to selectively predict a specific function, dysfunction, and activity of the ABC transporter family. Further the utility of claimed ABC, as postulated by applicant, consist of its potential role as an object of "use-testing".

Therefore the claimed ABC protein/DNA, is said to have a potential function based upon its amino acid sequence similarity to other known proteins. After further research, a specific and substantial credible utility might be found for the claimed polypeptide/DNA. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an

invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to a protein of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the claimed protein/polynucleotide was, as of the filing date, useful for breeding of a microorganism for the purpose of modifying transport of amino acids across a cell membrane. Further it is not clear what use it would be to breed a microorganism for the purpose of modifying transport of amino acids across a cell membrane. Until some actual and specific significance can be attributed to the claimed ABC protein/DNA, or the gene encoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

The ABC protein/DNA may share some structural similarity to the ABC transporter family based on undisclosed sequence similarity. As disclosed by the ABC transporter family may have diverse effects, and play roles in the pathogenesis of various diseases. Although the family ABC transporter proteins may share some common structural motifs to claimed ABC protein/DNA, various members of the family

may have different sites of action and different biological effects. In the absence of knowledge of the ligand for claimed invention or molecules transported, or the biological significance of the claimed ABC protein/DNA, there is no immediately evident patentable use. To employ the protein/DNA of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for claimed polypeptide, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful. Further there is no disclosure of what is the critical structure of the invention that is required for functionality.

The claimed ABC protein/DNA belongs is a family in which the members have divergent functions based on which tissues the protein is expressed or administered to. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. There are some protein families for which assignment of a new protein in that family would convey a specific, substantial and credible utility to that protein. For example, some families of enzymes such as proteases, ligases, telomerases, etc. share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family.

The diversity of the family of proteins, to which claimed ABC transporter is suggested to belong, has already been described. Without some common biological

activity for the family members, a new member would not have a specific, substantial, or credible utility when relying only on the fact that it has structural similarity to the other family members. The members of the family have different biological activities which may be related to tissue distribution but there is no evidence that the claimed compounds share any one of diverse number of activities. That is, no activity is known to be common to all members. Without knowing a biological significance of the claimed polypeptide/DNA, one of ordinary skill in the art would not know how to use the claimed invention in its currently available form in a credible "real world" manner based on the diversity of biological activities possessed by the ABC transporter family. Contrast *Brenner*, 148 USPQ at 694 (despite similarity with adjacent homologue, there was insufficient likelihood that the steroid would have similar tumor-inhibiting characteristics), with *In re Folkers*, 145 USPQ 390, 393 (CCPA 1965) (some uses can be immediately inferred from a recital of certain properties) or *In re Brana*, 34 USPQ 1436, 1441 (Fed. Cir. 1995) (evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility; here, an implicit assertion of a tumor target was sufficiently specific to satisfy the threshold utility requirement).

For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention. For reasons set forth above the disclosure satisfies none of the three criteria *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might

be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.')

Also, for reasons set forth above, Applicant has not presented sufficient evidence to support specific utility for ABC transporter or its variants. The present rejection under § 101 follows *Brenner v. Manson*, as set forth above. In that case, the absence of a demonstrated specific utility for the claimed steroid compound was not ameliorated by the existence of a demonstrated general utility for the class. Unlike *Fujikawa v. Wattanasin*, where there were pharmaceutically acceptable in vitro results, here, there is nothing other than relatively low levels of sequence homology to a broad and diverse family of proteins having distinct modes of activity, and no disclosed common mode of action. A rejection under § 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under § 101. *See, e.g., In re Swartz*, 56 USPQ2d 1703 (Fed. Cir. 2000); *In re Kirk*, 153 USPQ 48 (CCPA 1967).

3. Claim 7 remains rejected and newly added claims 15 and 16 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use

the claimed invention. Neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed polypeptide of SEQ ID NO:9 encoded by the polynucleotide of SEQ ID NO:7. The claims encompass polypeptides and polynucleotides and variants thereof which may be completely unrelated to the protein of SEQ ID NO:9 or DNA of SEQ ID NO:7, structurally and functionally, further even lacking the critical feature of the invention. Further experimentation is necessary to attribute a utility to the claimed nucleic acid/protein and variants thereof. Therefore claims 7, 15 and 16 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The claims are drawn to an orphan ABC transporter protein/DNA. The claimed nucleic acid encodes an orphan ABC transporter whose activity, compound transported, activating ligands and functionality have not been disclosed. Neither the claims nor the specification disclose what specific biological activity is associated with the claimed ABC transporter. There is no disclosure of the specific compounds that are transported, proteins activated in the signal transduction pathway or what ligand is capable of binding to the polypeptide encoded by the claimed polynucleotide, so as to disclose a specific function for the claimed polynucleotide. Therefore nucleic acid encoding unrelated and inactive proteins is encompassed by the claims. The specification does not disclose how to produce or isolate variants that transport the same compounds as

the claimed invention. Just because the protein has ATPase activity does not mean it will transport the same compounds as the transporter of SEQ ID NO:9. The specification has not disclosed an assay which will identify an ATPAase protein as being an ABC transporter belonging to the genus claimed, i.e. having the same substrate transport characteristics.

Therefore, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Claim Rejection 35 USC § 112, 1st paragraph (Written Description)

4. Claims 7 remains rejected and claim 15 is newly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims are claims 7 and 15 encompass variants which hybridize to nucleotides 1117-1725 of SEQ ID NO:7 or to probes (of undefined length) prepared from said nuclotide sequence.

Applicant argues the hybridization under stringent conditions clearly limits the variants of the sequence shown in SEQ ID N0. 9 and the stringent conditions of the hybridization will not produce polynucleotides that encode polypeptides which are completely unrelated to the polypeptide of SEQ ID NO. 9. Applicant also argues there

is clearly a common technical feature of the claimed invention, in that the novel gene/protein of the invention is useful as an ABC transporter. These proteins are known in the art for being able to transport amino acids into or out of a cell, as demonstrated by the evidence presented (see Arch Microbiol article). Therefore, one of ordinary skill in the art would be able to determine other hybridization variants by their common activity and critical special feature as an ABC transporter.

Applicant's arguments have been fully considered but are not found persuasive. Higgins, (IDS ref AAA) discloses that the designation ABC transporters recognizes a highly conserved ATP-binding cassette, which is the most characteristic feature of this superfamily but each ABC transporter is relatively specific for a given substrate. ABC transporters are specific for amino acids, sugars, inorganic ions, polysaccharides, peptides, and even proteins have been characterized (Table 1, see Higgins). Some ABC transporters are uptake (import) systems that accumulate substrate within the cell, while others export substrate from the cell. Further, on page 88, Higgins discloses, even close similarities between ABC transporters can be misleading: the Mal and Ugp transport systems of E. coli are closely related yet handle different substrates and the two human mdr genes are very similar to each other, yet only one is able to mediate drug transport.

The specification not prior art disclose the compounds transported by claimed transporter. The recitation of having ATPase transport is insufficient to describe the genus of compounds claimed. The crtical feature of the invention is that a specific structure, having an ATPase activity transports a specific compound. Without

knowledge of the compound transported it cannot be determined if a product is encompassed by the claimed species. Closely related ABC transporter, with ATPase activity, may handle different substrates.

The claims encompasses variants of the nucleic acid molecules of SEQ ID NO:7 encoding variants of the protein disclosed in SEQ ID NO:9, said variants may be completely unrelated, structurally and functionally to the protein encoded by SEQ ID NO:9 .

The common function of the nucleic acid (SEQ ID NO:7) encoding the polypeptide (SEQ ID NO:9), which is based upon a common property or critical technical feature of the genus claimed is not disclosed. What compound is transported by claimed genus of compounds or their encoded proteins? The claims, as written, encompass nucleic acid encoding polypeptides which vary substantially in length and also in amino acid composition. The instant disclosure of a polynucleotide of SEQ ID NO:7 encoding the polypeptide of SEQ ID NO:9 does not adequately describe the scope of the use of the claimed genus, which encompasses a substantial variety of subgenera including polynucleotides, proteins, variants of said polynucleotides and proteins, allelic variants, chimeric constructs, fusion constructs, variants and polynucleotides which hybridize to the nucleic acid of SEQ ID NO:7 or probes prepared from said nucleotide. Further said polynucleotide variants may encode polypeptides completely, unrelated functionally to the polypeptide of SEQ ID NO:9. A description of a genus of polypeptides may be achieved by means of a recitation of a representative number of polypeptides, defined by amino acid sequence, falling within the scope of the

genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Instant specification fails to provide sufficient descriptive information, such as definitive structural and functional features of the claimed genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. For example, what regions and fragments of the claimed VR-L contain a definitive structural feature required for protein function? The specification proposes to discover other members of the genus by using screening assays and techniques involving probes, primers, and hybridization. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides and proteins encompassed. No identifying characteristic or property of the instant polypeptides/polynucleotide is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific polypeptide and nucleotide sequences and the inability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude

that the disclosure fails to provide a representative number of species to describe, enable and use the genus as broadly claimed. The skilled artisan cannot envision the detailed chemical structure of the encompassed proteins and, therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. It is acknowledged that the skill of the artisan in the molecular biology art is high. However, in the current instance, there is no clear evidence of the compound transported by a protein with ATPase activity, which is encoded by the claimed genus of nucleic acid molecules. Since ATPase activity of ABC transporters does not differentiate one transporter from another, the description must also encompass the identity of the compound transported. How the critical special technical feature encompassed by the genus claimed relates to function must also be provided. Because of the lack of guidance in the prior art and current application, one skilled in the art could not predict if the claimed variants have the same activity as the protein disclosed in SEQ ID NO:9, since no transport activity is disclosed, or if they contain the domain(s) of SEQ ID NO:9, containing the critical special technical feature of the claimed transporter, since no critical special technical feature is disclosed. A transporter with different compound transport properties than that encoded by the polynucleotide of SEQ ID NO:7 may not useful for breeding of a microorganism for the purpose of modifying transport of amino acids across a cell membrane similar to that of claimed

invention. The specification does not disclose which amino acids encode the ATPase activity, and how structure is related to function.

Pertaining to variants to the nucleic acid/protein the skilled artisan cannot envision the detailed chemical structure of the encompassed compounds and, therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115). Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid or polypeptide is itself is required. See *Fibers v. Revel*, 25 USPQ d. 1601 at 1606 (CAFC 1993) and *Amen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic

acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". Therefore the specification fails to disclose the activity of the claimed genus of polypeptides/polynucleotides, the critical special technical feature of the polypeptides/polynucleotides or how the critical special technical feature encompassed by the fragments and variants of claimed ABC transporter relates to function. Similarly pertaining to nucleic acids which hybridize to the probes (of no disclosed size) polynucleotide of SEQ ID NO:7, what is the special technical feature encompassed by said nucleic acids and how do they relate to function. What is the minimum size of probe required to obtain functional transporter? What is the sequence of said probe?

The claims encompass nucleic acids encoding proteins which are structurally and functionally unrelated to the protein/nucleic acid disclosed in SEQ ID NO:9 and 7, respectively. Therefore instant specification fails to provide sufficient descriptive information, such as definitive structural/ functional features of the claimed genus of nucleic acids/polypeptides . There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no disclosure of the

specific activity of claimed ABC transporter and how it is specifically assayed for a specific compound transported. The specification nor claims disclose the specific activity of the claimed ABC transporter of instant invention nor a description of the conserved regions which are critical to the structure and function of the genus claimed.

There is no disclosure of the compound transported by the claimed genus nucleic acids encoding a claimed ABC transporter or the nature of the signal or specific signal transduction pathway. The claimed nucleic acid encodes an orphan ABC transporter whose activity, associated function and activating ligands have not been disclosed. The neither specification nor prior art provide a specific assay for the genus claimed. Nucleic acids/proteins comprising variants of claimed ABC transporter may be completely unrelated to the protein encoded by the nucleic acid of SEQ ID NO:7 The superfamily of ion transporters are specialized proteins designed for chemical recognition of ligands, transport of specific compounds, and subsequent transduction of information encoded in those ligands/compounds to the machinery of the cell. Ion transporters interact with many diverse compounds having diverse effects. The important features which would help to define the claimed ABC transporter activity and define the genus claimed have not been disclosed in the specification nor prior art.

The claims encompass nucleic acids encoding proteins which are structurally and functionally unrelated to the protein of SEQ ID NO:9. Therefore instant specification fails to provide sufficient descriptive information, such as definitive structural/ functional features of the claimed genus of polypeptides/polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus

claimed. The neither specification nor claims disclose the specific activity of the "orphan claimed ABC transporter " of instant invention, how it is assayed, nor a description of the conserved regions which are critical to the structure and function of the genus claimed. Therefore, for reason given above, claims 7 and 15 are rejected.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nirmal s. Basi
Art Unit 1646
September 30, 2004

Brenda Brumback
BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600